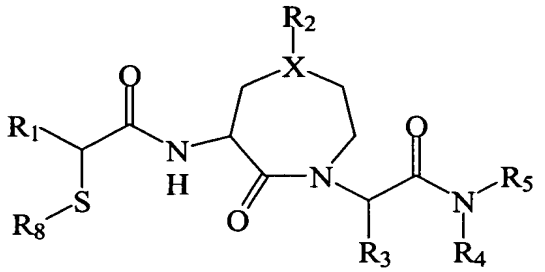
LISTING OF CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Currently Amended) A compound of the formula



(1)

wherein

R_1 is C_1-C_6 alkyl, a W-$(CH_2)_m$- group, or a Q-Z-$(CH_2)_m$- group wherein W is phthalimido; Z is a bond or is oxy, NR_6, $C(O)NR_6$, $NR_6C(O)$, $NHC(O)NR_6$, $OC(O)NR_6$, HNC(O)O, or SO_2NR_6; Q is hydrogen, or a Y-$(CH_2)_n$- group wherein Y is hydrogen, C_6-C_{10} aryl, ~~C_3-C_9 heteroaryl~~ a cyclic or bicyclic, aromatic assemblage of three to nine carbon atoms and from 1 to 3 nitrogen, oxygen, or sulfur atoms, -$C(O)OR_6$, -$N(R_6)_2$, morpholino, piperidino, pyrrolidino, or isoindolyl;

R_2 is C_1-C_4 alkyl, a -$(CH_2)_p$-(C_3-C_9)heteroaryl group, or a -$(CH_2)_p$-Ar_1 group wherein Ar_1 is phenyl or naphthyl optionally substituted with a substituent selected from the group consisting of halogen, C_1-C_4 alkyl, -OR_7, -$N(R_6)_2$, $SO_2N(R_6)_2$ or -NO_2;

R_3 is hydrogen, C_1-C_6 alkyl, -$CH_2SCH_2NHCOCH_3$, a -$(CH_2)_p$-A group, a -$(CH_2)_m$-B group or a -CH_2-D-R_7 group wherein A is C_6-C_{10} aryl, C_3-C_9 heteroaryl, or cyclohexyl; B is -$N(R_7)_2$, guanidino, nitroguanidino, -$C(O)OR_6$ or -$C(O)NR_6$; and D is oxy or thio;

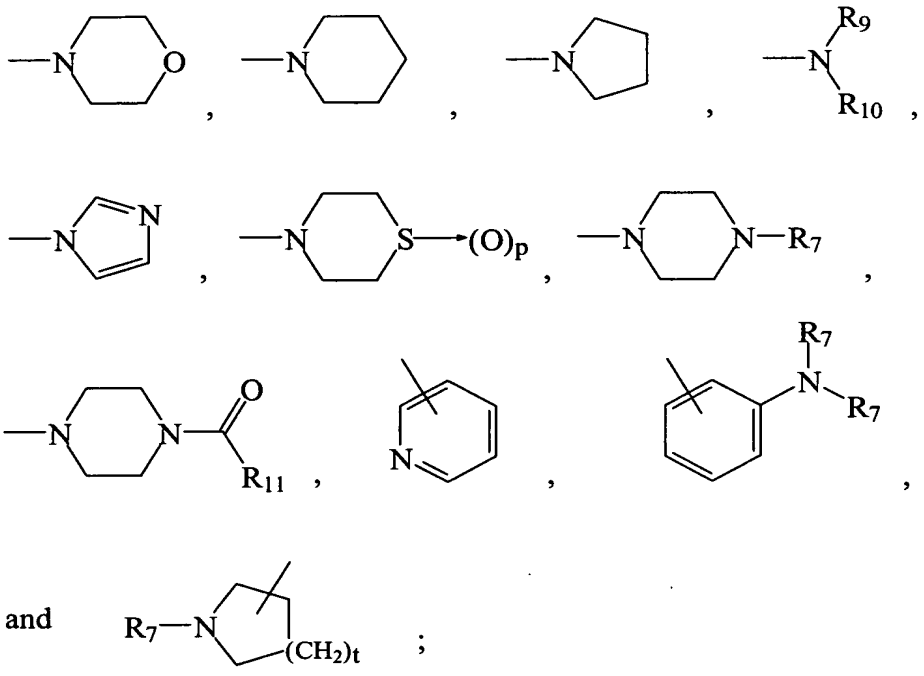
R_4 is hydrogen or a -$(CH_2)_m$-$S(O)_pX'(R_6)_2$ group;

R_5 is hydrogen, C_1-C_6 alkyl or R_4 and R_5 taken together with the nitrogen atom to which they are attached form piperidino, pyrrolidino, or isoindolyl;

R_6 is hydrogen or C_1-C_6 alkyl;

R_7 is hydrogen, C_1-C_4 alkyl, or a $-(CH_2)_p-Ar_2$ group wherein Ar_2 is phenyl or naphthyl optionally substituted with a substituent selected from the group consisting of halogen, C_1-C_4 alkyl, $-OR_7$, $-N(R_6)_2$, $SO_2N(R_6)_2$ or $-NO_2$;

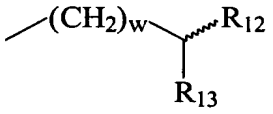
R_8 is hydrogen, $-C(O)R_7$, a $-C(O)-(CH_2)_q-K$ group or a -S-G group, wherein K is selected from the group consisting of



and

;

G is selected from the group consisting of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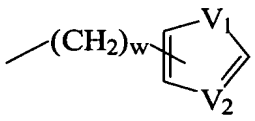
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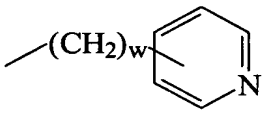
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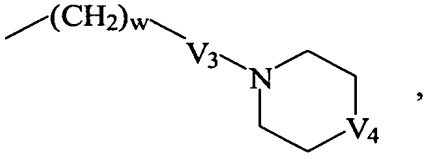
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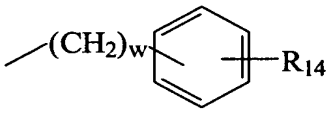
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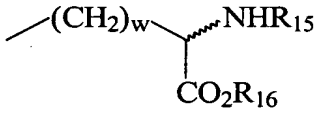
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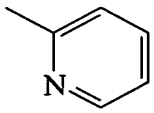

;

R_9 and R_{10} are each independently C_1-C_4 alkyl or a -$(CH_2)_p$-Ar_2 group;

R_{11} is -CF_3, C_1-C_{10} alkyl or a -$(CH_2)_p$-Ar_2 group;

R_{12} is hydrogen, C_1-C_6 alkyl, -$CH_2CH_2S(O)_pCH_3$, or arylalkyl;

R_{13} is hydrogen, hydroxy, amino, C_1-C_6 alkyl, N-methylamino, N,N-dimethylamino,

-CO_2R_{17} or -$OC(O)R_{18}$ wherein R_{17} is hydrogen, -CH_2O-$C(O)C(CH_3)_3$, C_1-C_4 alkyl, a

-$(CH_2)_p$-Ar_2 group or diphenylmethyl and R_{18} is hydrogen, C_1-C_6 alkyl or phenyl;

R_{14} is 1 or 2 substituents independently chosen from the group consisting of hydrogen,

C_1-C_4 alkyl, C_1-C_4 alkoxy, or halogen;

R_{15} is hydrogen, C_1-C_6 alkyl or a -$(CH_2)_p$-Ar_2 group;

R_{16} is hydrogen or C_1-C_4 alkyl;

V_1 is O, S, or NH;

V_2 is N or CH;

V_3 is a bond or -C(O)-;

V_4 is $-(CH_2)_{w'}-$, O, S, NR_7, or $NC(O)R_{11}$;

X and X' are each independently CH or N;

m is an integer 2-4;

n is zero or an integer 1-4;

p is zero or an integer 1-2;

q is zero or an integer 1-5;

t is an integer 1-2;

w is an integer 1-3; and

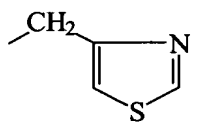
w' is zero or an integer 1; or

a pharmaceutically acceptable salt, stereoisomer or hydrate thereof.

2. (Original) A compound of claim 1 wherein X is CH.

3. (Original) A compound of claim 2 wherein R_2 is C_1-C_4 alkyl or a $-(CH_2)_p$-Ar group wherein Ar is phenyl optionally substituted with F, Cl, C_1-C_4 alkyl, $-NO_2$, $-NH_2$ or $-OR_7$; and R_4 is hydrogen.

4. (Previously Presented) A compound of claim 3 wherein R_3 is hydrogen, C_1-C_6 alkyl, phenyl, benzyl, 1-naphthyl, 2-naphthyl, cyclohexylmethyl, 2-hydroxyphenyl, 3-hydroxyphenyl, 4-hyroxyphenyl, 2,3-dihydroxyphenyl, 2,4-dihydroxyphenyl, 3,4-dihydroxyphenyl, 4-methoxyphenyl, 4-ethoxyphenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 3,4-dichlorophenyl, 4-bromophenyl, 3,4-dibromophenyl, 4-fluorophenyl, 3,4-difluorophenyl, 3-tolyl, 4-tolyl, 4-ethylphenyl, 4-isopropylphenyl, 3-aminophenyl, 4-aminophenyl, 3,4-diaminophenyl, N-methyl-4-aminophenyl, 2-nitrophenyl, 4-nitrophenyl, 4-aminobenzyl, 4-hydroxybenzyl, 4-methoxybenzyl, 3-chlorobenzyl, 4-fluorobenzyl, 3,4-dichlorobenzyl, 4-bromobenzyl, 4-methylbenzyl, or is a compound of the formula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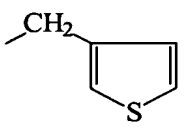
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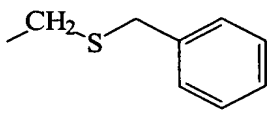
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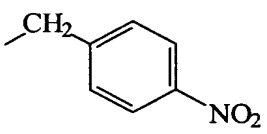
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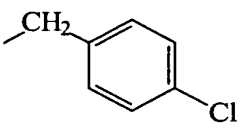
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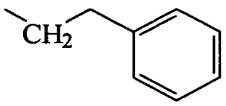
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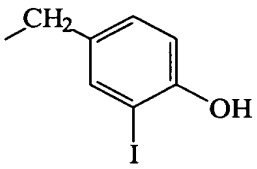
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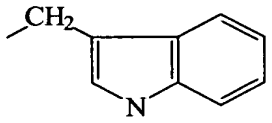
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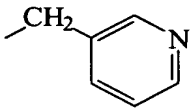
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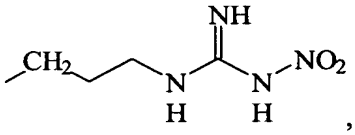
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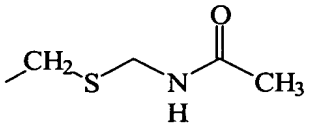
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5. (Original) A compound of claim 4 wherein R_5 is hydrogen, methyl, ethyl, propyl, isopropyl, butyl or isobutyl and R_8 is hydrogen.

6. (Original) A compound of claim 2 wherein R_1 is a W-$(CH_2)_m$- group.

7. (Original) A compound of claim 3 wherein R_1 is a W-$(CH_2)_m$- group.

8. (Original) A compound of claim 5 wherein R_1 is a W-$(CH_2)_m$- group.

9. (Original) A compound of claim 2 wherein R_1 is C_1-C_6 alkyl.

10. (Original) A compound of claim 3 wherein R_1 is C_1-C_6 alkyl.

11. (Original) A compound of claim 5 wherein R_1 is a C_1-C_6 alkyl.

12. (Original) A compound of claim 2 wherein R_1 is a Q-Z-$(CH_2)_m$- group.

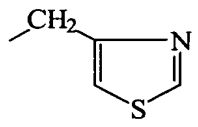
13. (Original) A compound of claim 3 wherein R_1 is a Q-Z-$(CH_2)_m$- group.

14. (Original) A compound of claim 5 wherein R_1 is a Q-Z-$(CH_2)_m$- group.

15. (Original) A compound of claim 1 wherein X is N.

16. (Original) A compound of claim 15 wherein R_2 is C_1-C_4 alkyl or a -$(CH_2)_p$-Ar group wherein Ar is phenyl optionally substituted with F, Cl, C_1-C_4 alkyl, -NO_2, -NH_2 or -OR_8; and R_4 is hydrogen.

17. (Previously Presented) A compound of claim 16 wherein R_3 is hydrogen, C_1-C_6 alkyl, phenyl, benzyl, 1-naphthyl, 2-naphthyl, cyclohexylmethyl, 2-hydroxyphenyl, 3-hydroxyphenyl, 4-hyroxyphenyl, 2,3-dihydroxyphenyl, 2,4-dihydroxyphenyl, 3,4-dihydroxyphenyl, 4-methoxyphenyl, 4-ethoxyphenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 3,4-dichlorophenyl, 4-bromophenyl, 3,4-dibromophenyl, 4-fluorophenyl, 3,4-difluorophenyl, 3-tolyl, 4-tolyl, 4-ethylphenyl, 4-isopropylphenyl, 3-aminophenyl, 4-aminophenyl, 3,4-diaminophenyl, N-methyl-4-aminophenyl, 2-nitrophenyl, 4-nitrophenyl, 4-aminobenzyl, 4-hydroxybenzyl, 4-methoxybenzyl, 3-chlorobenzyl, 4-fluorobenzyl, 3,4-dichlorobenzyl, 4-bromobenzyl, 4-methylbenzyl, or is a compound of the formula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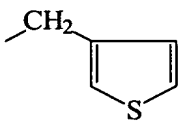
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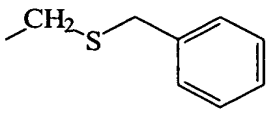
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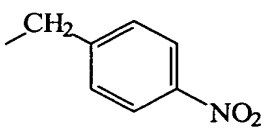
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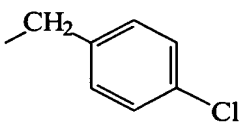
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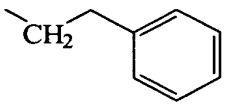
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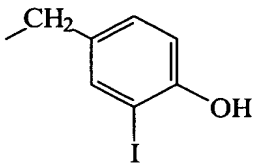
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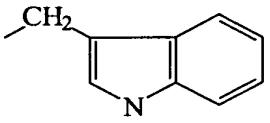
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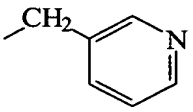
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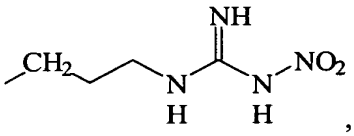
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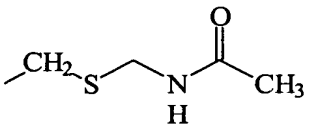
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18. (Original) A compound of claim 17 wherein R_5 is hydrogen, methyl, ethyl, propyl, isopropyl, butyl or isobutyl and R_8 is hydrogen.

19. (Original) A compound of claim 16 wherein R_1 is a W-$(CH_2)_m$- group.

20. (Original) A compound of claim 17 wherein R_1 is a W-$(CH_2)_m$- group.

21. (Original) A compound of claim 19 wherein R_1 is a W-$(CH_2)_m$- group.

22. (Original) A compound of claim 16 wherein R_1 is C_1-C_6 alkyl.

23. (Original) A compound of claim 17 wherein R_1 is C_1-C_6 alkyl.

24. (Original) A compound of claim 19 wherein R_1 is a C_1-C_6 alkyl.

25. (Original) A compound of claim 16 wherein R_1 is a Q-Z-$(CH_2)_m$- group.

26. (Original) A compound of claim 17 wherein R_1 is a Q-Z-$(CH_2)_m$- group.

27. (Original) A compound of claim 19 wherein R_1 is a Q-Z-$(CH_2)_m$- group.

28. (Original) A compound of claim 1 wherein X is CH; R_2 is phenyl, methyl or ethyl; R_3 is phenyl, benzyl, cyclohexylmethyl, isopropyl, isobutyl, 3-pyridylmethyl, 4-fluorobenzyl or 4-aminobenzyl; R_4 is hydrogen; R_5 is hydrogen, methyl, ethyl, propyl, isopropyl, butyl or isobutyl and R_8 is hydrogen.

29. (Original) A compound of claim 28 wherein R_1 is a W-$(CH_2)_m$- group.

30. (Original) A compound of claim 1 wherein X is N; R_2 is phenyl, methyl or ethyl; R_3 is phenyl, benzyl, cyclohexylmethyl, isopropyl, isobutyl, 3-pyridylmethyl, 4-fluorobenzyl or 4-aminobenzyl; R_4 is hydrogen; R_5 is hydrogen, methyl, ethyl, propyl, isopropyl, butyl or isobutyl and R_8 is hydrogen.

31. (Original) A compound of claim 30 wherein R_1 is a W-$(CH_2)_m$- group.

32. (Original) A compound of claim 1 wherein said compound is 2*H*-Isoindole-2-hexanamide, *N*-[hexahydro-1-[2-(methylamino)-2-oxo-1-(phenylmethyl)ethyl]-2-oxo-5-phenyl-1*H*-azepin-3-yl]-1,3-dihydro-α-mercapto-1,3-dioxo-, [3*S*-[1(*R**), 3α, 5α]]-.

33. (Original) A compound of claim 1 wherein said compound is 2*H*-Isoindole-2-hexanamide, *N*-[hexahydro-1-[2-(methylamino)-2-oxo-1-(phenylmethyl)ethyl]-2-oxo-5-phenyl-1*H*-azepin-3-yl]-1,3-dihydro-α-mercapto-1,3-dioxo-, [3*S*-[1(*R**), 3α, 5β]]-.

34. (Original) A compound of claim 1 wherein said compound is 2*H*-Isoindole-2-hexanamide, *N*-[hexahydro-4-[2-(methylamino)-2-oxo-1-(phenylmethyl)ethyl]-5-oxo-1-(phenylmethyl)-1*H*-1,4-diazepin-6-yl]-1,3-dihydro-α-mercapto-1,3-dioxo-, [6*S*-[4(*R**), 6*R**(*R**)]]-.

35. (Original) A pharmaceutical composition comprising a compound of claim 1 and a pharmaceutically acceptable carrier.

36. (Cancelled)

37. (Cancelled)

38. (Original) A method of treating rheumatoid arthritis in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

39. (Original) A method of treating osteoarthritis in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

40. (Original) A method of treating a chronic inflammatory disorder in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

41. (Cancelled)

42. (Cancelled)

43. (Original) A method of claim 42 wherein said cardiovascular disorder is atherosclerosis.

44. (Original) A method of treating corneal ulceration in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

45. (Original) A method of treating gingivitis or periodontal disease in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

46. (Cancelled)

47. (Original) A method of treating chronic obstructive pulmonary disorder in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.